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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,183	06/30/2005	Berndt Oberhauser	PD/4-32540A	6151

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
KIFLE, BRUCK	

ART UNIT	PAPER NUMBER
1624	

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07/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,183	OBERHAUSER ET AL.	
	Examiner	Art Unit	
	Bruck Kifle, Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 7-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8-10,13,15-19 and 26-29* is/are rejected.

7)☒ Claim(s) *2-7,11,12,14 and 22-25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's amendments and remarks filed 04/04/07 have been received and reviewed. Claims 1-4 and 7-29 are now pending in this application.

Claim Rejections - 35 USC § 112

Claims 1, 10, 15, 16 and 18-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

i) In claim 1 the definition of R_2 is unclear. The definition is reproduced below.

R_2 is unsubstituted (C_{1-4})alkyl or (C_{1-4})alkyl substituted by unsubstituted or substituted
- (C_{6-18})aryl or
wherein the substitutients are
- quinolinyl,
- benzo[1,3]dioxolyl,
- phenyl,
- phenyl one or morefold substituted by halogen, halo(C_{1-4})alkyl, (C_{1-4})alkoxy, cyano, amino, dimethylamino, carboxy (C_{1-2})alkylcarbonylamino, amino(C_{1-2})alkylcarbonylamino, (C_{2-4})alkylenecarbonylamino, or heterocyclylcarbonyl(C_{1-2})alkylcarbonylamino, wherein heterocyclyl has 6 ring members and 2 heteroatoms selected from N, and O;
- (C_{6-18})aryl annelated with heterocyclyl having 5 or 6 ring members and 1 to 4 heteroatoms selected from N, O, and S;~~and~~
wherein the substituents are
- halogen
- unsubstituted amino or amino substituted by one or two (C_{1-4}) alkyl,
- cyano
- (C_{1-4}) alkoxy, or
- (C_{1-8}) haloalkyl, and

First, the term "or" should be at the end of the first definition of R_2. It is suggested to more clearly set forth that the group R_2 is also a (C_{1-4})alkyl substituted by an (C_{6-18}) aryl annelated with a heterocyclyl which is substituted by the groups halogen, amino, cyano, etc. as listed above if this is what Applicants intention is.

ii) Claim 18, which is a method claim, improperly depends from claim 8, which is drawn to a pharmaceutical composition. See also, claim 19 which depends from claim 18.

iii) In claims 8, 10, 15, 16 and 18-21, the compounds active in "immunodulating regimens or other anti-inflammatory agents" are not known. These claims are of a different scope.

Note that compounds, corresponding compositions, a method of use and a process of making that are of the **same scope** are considered to form a single inventive concept under PCT Rule 13.1, 37 CFR 1.475(d). These claims are not so linked as to form a single inventive concept.

Claims 9, 10, 13, 15-21 and 26-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for treating inflammatory diseases, allergic conditions, autoimmune diseases, transplantation rejections graft vs. host disease, neoplastic diseases, or infectious diseases generally.

The specification does not enable any physician skilled in the art of medicine, to use the invention commensurate in scope with these claims. The factors to be considered in making an enablement rejection have been summarized below.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Claims 9 and 10 are drawn to treating inflammatory diseases, allergic conditions, autoimmune diseases or transplantation rejection. Claims 13-16 depend on claims 9 or 10 and list a number of diseases. Claim 17 is drawn to treating graft vs. host disease, neoplastic diseases, or infectious diseases. Claims 26-29 depend from claim 9 and limit the compound used.

2) The state of the prior art: There is no single compound that can treat any and all of the diseases recited.

The scope of the claims includes treating any or all neoplastic diseases. No compound has ever been found that can treat all neoplastic diseases even though massive efforts have been directed towards this end. Since this assertion is contrary to what is known in oncology, proof must be provided that this revolutionary assertion has merits. Nearly all-antineopastic drugs are effective against only a limited group of related neoplastic diseases. Therefore, a compound effective against all neoplastic diseases would be a revolutionary exception. Applicant is asserting that he succeeded where others have failed. Where extensive efforts have all failed, it is reasonable for the Patent and Trademark Office to require proof that the claimed invention actually works for this specific utility. It is well established that a utility rejection is proper when scope of enablement is not reasonably correlated to the scope of the claims. (In re Vaeck 20 USPQ2d 1439, 1444, In re Ferens 163 USPQ 609).

In re Buting 163 USPQ 689 establishes that even clinical tests showing that a compound found to be useful in the treatment of two types of cancers was not sufficient for a much broader range.

Inflammation is a process that can take place in virtually any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the inflammatory reaction. There is no common mechanism by which all, or even most, inflammations arise. Mediators include bradykinin, serotonin, C3a, C5a, histamine, leukotrienes, cytokines, and many, many others. Accordingly, treatments for inflammation are normally tailored to the particular type of inflammation present, as there is no, and there can be no "magic bullet" against inflammation generally.

Regarding multiple sclerosis, interferon is the only established therapy for multiple sclerosis. Glatiramer acetate is a second line treatment used in the US but not Europe. Thus, the skilled clinician would not know how to use Applicants' compounds to treat MS.

Infectious diseases include HIV/AIDS, TB, malaria, measles, tetanus, meningitis, hepatitis, etc. The notion that a single drug could be effective against infectious diseases is prima facie not enabled.

The treatment of "autoimmune diseases" generally would be unprecedented feat. For a compound or genus to be effective against "autoimmune diseases" generally is contrary to medical science. The "autoimmune diseases" are a process that can take place in virtually any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the inflammatory reaction. There are hundreds of such diseases, which have fundamentally different mechanisms and different underlying causes. There are both chromic and acute "autoimmune diseases", most of which lack satisfactory treatment. The intractability of these disorders is clear evidence that the skill level in this art is low relative to the difficulty of the task. Under such circumstances, it is proper for the PTO to

require evidence that such an unprecedented feat has actually been accomplished, In re Ferens, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, Genentech vs. Novo Nordisk, 42 USPQ2nd 1001, 1006.

What guidance does the specification offer the clinician in the use of Applicants' compounds for treating of any and al of these diseases?

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for treating any or all condition of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended host. Moreover many if not most of diseases such as psoriasis and cancers, MS, infectious diseases, etc. are very difficult to treat.

Case law is clear on this point. In an unpredictable art, such as MS therapy, models may be used for enablement only if there is a well-established correlation between the assay and clinical efficacy.

The specification has no working examples to show treating any or all condition and the state of the art is unpredictable.

6) The breadth of the claims: The instant claims embrace treating any and all inflammatory diseases, infectious diseases and neoplastic diseases, to name a few catagories.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of enzyme-inhibitor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP 2164.0l(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Claim 1 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action.

Claims 2-7, 11, 12, 14 and 22-25 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

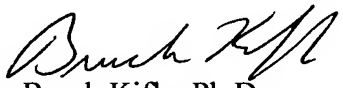
Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruck Kifle, Ph.D. whose telephone number is 571-272-0668. The examiner can normally be reached Mondays to Fridays between 8:30 AM and 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Bruck Kifle, Ph.D.
Primary Examiner
Art Unit 1624

BK
July 21, 2007